Zoonotic Marine Helminths: Anisakid Nematodes and Diphyllobothriid Cestodes

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1 Zoonotic Marine Nematodes: *Anisakis* Spp., *Pseudoterranova* Spp., and *Contracaecum* Spp.

1.1 Morphological and Genetic Information

The genus *Anisakis* (Dujardin 1845) refers to a group of nematodes with shared morphological characteristics. Recent molecular technological advances recognize species belonging to this genus: *A. pegreffii*, *A. simplex* s.s., *A. simplex* C, *A. typica*, *A. ziphidarum*, *A. physeteris*, *A. brevispiculata*, and *A. paggiae* with two distinct clades molecularly and based on morphological features (Matiiucci and Nascetti 2006). Clade I includes *A. simplex* sensu stricto, *A. pegreffii, A. simplex C, A. typica*, and *A. ziphidarum*, and Clade II includes *A. physeteris, A. brevispiculata*, and *A. paggiae*. The zoonotic condition "anisakiasis" is herein defined as human disease associated with nematode larvae and has been associated with a number of marine nematodes in addition to *Anisakis* spp., e.g., *Pseudoterranova* spp. and *Contracaecum* spp. (Myers 1976; Mehrdana et al. 2014). In tissue sections, ascarids such as *Anisakis* spp. and *Pseudoterranova* spp. are large nematodes with adults found within the stomach of definitive hosts and larvae present in any tissue section. Lateral alae and a thick cuticle are characteristic features, although not always present in larval ascarids, along with coelomyarian musculature that projects far into the body cavity (pseudocoelom), prominent lateral chords, and an esophagus lined by a uninucleate cuboidal to columnar layer of cells with a brush border (Gardiner and Poynton 1999). Species determination often requires microscopic and/or molecular testing.

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1.2 Life Cycle

The typical location of adult *Anisakis* spp. and *Anisakis*-like parasites is within the stomach of marine mammals (Fig. 1) from ingestion of larval stages within paratenic or intermediate invertebrate (e.g., squid and crustaceans) and vertebrate (e.g., fish) hosts (Smith and Wooten 1978). Definitive hosts of *Anisakis* spp. and *Pseudoterranova* spp. are typically marine mammals (e.g., cetaceans and pinnipeds), whereas birds are more commonly hosts to *Contracaecum* spp., where the adult nematodes develop within the digestive tract and adult female nematodes shed eggs in the feces of the definitive hosts. The eggs embryonate within the aquatic environment and the second-stage larvae are consumed by crustaceans (e.g., krill) that act as

Fig. 1 Examples of adult *Anisakis* sp. nematodes recovered from the stomach of a definitive host, the harbor porpoise (*Phocoena phocoena*), demonstrating the size and gross morphology. The nematodes were not associated with significant pathology in the porpoise. (photo courtesy of Dr. Gary Conboy, Atlantic Veterinary College)

the first intermediate hosts. The crustaceans are then consumed by the second intermediate hosts (i.e., fish or squid) where the third larval stage of the parasite encysts to be consumed by the definitive host to complete the cycle (Sakanari and McKerrow 1989). Humans can act as dead-end hosts for the parasite from ingestion of the infective larvae in the intermediate hosts, but the nematodes do not mature within the intestines of humans (Arriaza et al. 2010).

1.3 Pathology in Wild Animals

Severe ulceration and chronic inflammation of the gastrointestinal tract has been reported in many free-ranging species infected with ascarid nematodes with occasional gastric perforation, peritonitis, and death associated with infection, presumably in an aberrant or nontypical host (Fig. 2) (Nemeth et al. 2012; Wagner et al. 2012). Changes in species distributions related to climate change and other factors could result in an expansion of the host range of these parasites (Shamsi et al. 2017). Severe infection of *A. simplex* larvae in Atlantic salmon can be associated with hemorrhage and inflammation around the vent that has been termed "red vent syndrome," with anglers first noticing and reporting the condition (Larrat et al. 2013; Noguera et al. 2009). The presence of the parasite within the muscles of

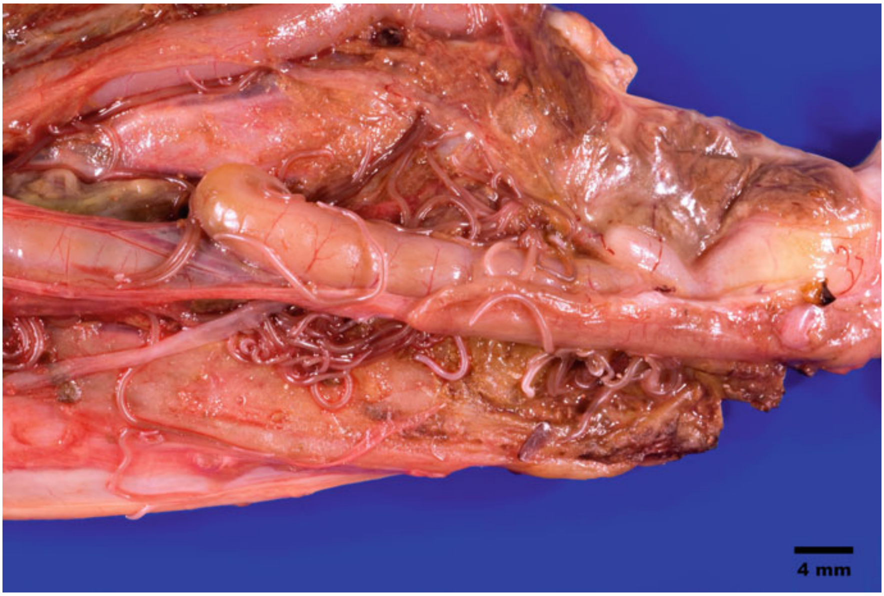

Fig. 2 Gross image of the gastrointestinal tract from a greater shearwater (*Puffinus gravis*) found dead off the coast of Georgia, U.S.A., that suffered fatal peritonitis due to an *Anisakis* sp. infection. Multiple adult nematodes are present in the image associated with proventricular rupture and coelomitis (inflammation within the abdominal cavity). (photo courtesy of Dr. Kevin Keel and the Southeastern Cooperative Wildlife Disease Study)

European smelt (*Osmerus eperlanus*) and eel (*Anguilla anguilla*) has been associated with increased mortality, presumably due to impairment of swimming ability caused by the nematodes (Sprengel and Lüchtenberg 1991).

1.4 Human Health Impacts

Humans develop anisakiasis from the consumption of raw, undercooked, smoked, or dried second intermediate hosts. Symptoms in humans can range from minimal to severe gastrointestinal disease that includes abdominal pain, nausea, vomiting, abdominal distention, diarrhea, and fever with occasional migration of larvae through other body systems such as the respiratory system with coughing, pharyngeal pain, and even the presence of larvae within sputum (Noh et al. 2003). Nasal and anal itching (pruritus) have also been reported. Severe infections can result in obstructions of the alimentary tract that have to be corrected surgically (Yoon et al. 2004). Gastrointestinal disease is also reported with *Pseudoterranova* sp. and *Contracaecum* sp. infections in humans; although these genera have not been as well studied as *Anisakis* sp., the clinical disease in humans is considered to be similar to that observed with *Anisakis* sp. infection, and all nematodes are lumped into the generic syndrome of "anisakiasis" with speciation likely requiring molecular analysis of the parasites (Weitzel et al. 2015). The *Anisakis* sp. nematodes can induce allergic reactions associated with exposure, and infected human patients are known to have elevations in serum IgE and eosinophilia, as well as potentially suffering from skin rashes, urticaria (hives), airway obstruction, and anaphylaxis (Perteguer et al. 2000; Nieuwenhuizen et al. 2006; Ludovisi et al. 2017; Mehrdana and Buchmann 2017). The pathogenesis of clinical disease in humans of both gastrointestinal and allergic reactions is thought to be associated with specific excretory and secretory proteins produced by the parasite (Mehrdana and Buchmann 2017). *Anisakis* spp. can be inactivated with prolonged freezing periods (i.e., below −20 °C for 7 days or below −35 °C for 15 h) and with cooking (56 °C for 5 min) (FDA 1998; Wharton and Aalders 2002). Prolonged salting can kill anisakid larvae, but some marinating procedures may not be sufficient for inactivation (Karl et al. 1994). Specific information on the effect of drying and smoking techniques on the survival of these parasites is not available. Larval nematodes can be removed from fillets, but sometimes, the fillets need to be cut deep or candled to detect the larvae. The identified allergens associated with anisakid nematodes are not destroyed with cooking or freezing and do not require previous exposure to elicit a reaction (Audicana et al. 1997).

1.5 Geographical Information

Members of the *Anisakis* genus, as well as similar nematodes of the *Pseudoterranova* and *Contracaecum* genera, can be found globally in many oceans worldwide, especially in areas with colder water. The species that is most common within circumpolar oceans is *Anisakis simplex* s. s. Human cases of anisakiasis have been reported in Europe, North America, Asia, and South America (Oshima 1972).

1.6 Relevance to Arctic Ecosystems

Climatic changes are warming Arctic Ocean temperatures, which are changing marine ecosystems in multiple ways, including an increase in the amount of freshwater. This can decrease salinity and alter pH, oxygenation, and other parameters thought to influence the environmental survival and development of anisakid eggs and larvae (Rokiki 2009). As the parasites can be found worldwide and infect a wide range of migratory hosts (fish, mammals, and birds), there are likely to be changes in species distributions and potential for emergence and re-emergence of zoonotic diseases associated with the consumption of raw or undercooked fish. The presence of the parasites would also be relevant to any commercial harvest of marine species since a high prevalence of these parasites would likely result in decreased quality of the products. Although these nematodes are not easily detected with the naked eye, processors are trained to detect them, and may utilize techniques such as candling or trimming fillets and removing the larvae manually (Levsen et al. 2005).

2 Zoonotic Marine Diphyllobothriid Cestodes; *Dibothriocephalus* spp. (Formerly *Diphyllobothrium* spp.)

2.1 Morphological and Genetic Information

There are approximately 80 species of *Dibothriocephalus* spp. (formerly *Diphyllobothrium* spp.) cestodes or tapeworms documented worldwide, with 15 species known to infect humans that are often referred to as the "fish tapeworm" or the "broad tapeworm." Infection in humans as a zoonosis is associated with the consumption of larvae (plerocercoids) within the flesh of marine and freshwater fish (Chai et al. 2005). The most common species associated with human infections worldwide are *D. latum* and *D. dendriticum* from freshwater fish and *D. pacificum* from saltwater fish (Sagua et al. 2001). The most common species with a holarctic distribution is *D. dendriticum*, with a number of other species documented in humans, specific documented infections in Alaska have included *D. alascense*, *D. dalliae*, and *D. ursi.* In addition to *D. dendriticum* and *D. latum*, infections with *D. nihonkaiense*, and *D. lanceolatum* and related tapeworms from other genera (*Pyramicocephalus phocarum* and *Schistocephalus solidus*) are known to infect humans living in cold climates (Scholz et al. 2009; Scholz and Kuchta 2016). Parasites are not always recovered and speciated from all infections, particularly in more remote and lower-income areas. Anadromous fish (fish that have freshwater and saltwater components in their life cycles), such as salmonids, can also act as intermediate hosts of the parasite and are commonly consumed by people. In tissue sections, cestodes have characteristic features that include segmentation into proglottids with both male and female components (hermaphrodite), as well as numerous eggs present in the adult worms, the absence of a body cavity or pseudocoelom, and instead the presence of a parenchymatous body with embedded calcareous corpuscles that is surrounded by a thin tegument (Gardiner and Poynton 1999). The larval and adult stages of *Diphyllobothrium* spp. have a scolex with grooves (referred to as bothria) that the parasite uses to attach to host tissue. Variability in the number and position of the scolex and bothria are often used to differentiate different species. The operculate, unembryonated eggs are 55–75 by 40–55 μm and have a small lobe at the end opposite the operculum.

2.2 Life Cycle

Dibothriocephalus spp. (formerly *Diphyllobothrium* spp.) begin as eggs that are shed into water bodies mature under appropriate environmental conditions, a process that takes approximately 18–20 days, and then develop into the free-swimming first larval stage (a coracidium) that, when ingested by a crustacean intermediate host (often a copepod), develops into the second larval stage (a procercoid). The crustacean host is then ingested by a second intermediate host (typically a freshwater or anadromous salmonid fish), and the tapeworm matures into a plerocercoid within the flesh, often muscle tissue of that fish. When the flesh of the second intermediate host is ingested by a definitive host thought to be a fish-eating (piscivorous) carnivore (e.g., cetacean, pinniped, felid, or canid) or bird, the cestode matures into an adult tapeworm within the small intestine (Bazsalovicsová et al. 2020). Other predatory fish (e.g., sharks) can act as parantenic hosts and develop plerocercoids within the flesh that could also be consumed by a piscivorous mammal. Humans can act as a definitive host of the parasite and are infected by consuming raw or undercooked (including smoked or dried) fish meat that is infected with plerocercoid larvae (Meyer 1970). The adult cestodes can grow very long (Fig. 3) (up to 11 m from a human in Chile) (Cabello 2007).

2.3 Pathology in Wild Animals

The intermediate and parantenic hosts (e.g. free-ranging fish) will have subcutaneous and intramuscular tissue cysts containing a plerocercoid larva that can be detected at necropsy or in harvested animals. These cysts may be surrounded by variable amounts of fibrous connective tissue and small amounts of inflammatory cells. In addition to higher trophic level marine mammals, birds, and humans, other potential definitive hosts can include other carnivores such as canids, bears, felines, and otters (Bazsalovicsová et al. 2020; Cabrera et al. 2001). Limited specific information on the impact of cestode infections on free-ranging mammals exists as it is likely that many species have coevolved for millennia with these parasites. However, the clinical syndromes reported in people, including gastrointestinal signs and competition for host nutrients, could presumably also negatively impact other mammalian hosts in

Fig. 3 Preserved adult diphyllobothriid cestode removed from a human patient from the mainland United States with no travel history. (Photo courtesy of Dr. Sarah G. H. Sapp, Parasitic Diseases Branch, Centers for Disease Control and Prevention)

cases of severe infection. This may be relevant in the face of other cumulative impacts associated with food availability, stress, pollutants, other infectious diseases, habitat loss, climate change, and resource development.

2.4 Human Health Impacts

Zoonotic cestodes thought to be *D. pacificum* have been detected in the intestinal tract of mummified ancient humans and coprolites (fossilized feces) from Huaca, Peru, from approximately 4500 BP, from coastal Chile from approximately

6060–3900 BP, and in Germany in 6000 BP (Callen and Cameron 1960; Reinhard and Aufderheide 1990; Reinhard and Urban 2003; Le Bailly and Bouchet 2013). In 1973, it was estimated that 9 million persons were infected globally with known endemic regions of high prevalence in Sweden, Finland, and Russia (von Bonsdorff 1977). Diphyllobothriasis is currently considered the most significant food-borne parasite from fish with current estimates of worldwide human cases exceeding 20 million. Infections by zoonotic nematodes in humans can range from asymptomatic to severe flu-like illness with abdominal cramps, flatulence, abdominal distention, diarrhea, and induced vitamin B_{12} insufficiency due to malabsorption and even megaloblastic anemia (Baer 1969; von Bonsdorff 1977; Ito and Budke 2014). Although diphyllobothriasis can affect any age and sex, middle-aged men are overrepresented. A few studies have specifically examined the number of cases in Arctic peoples in Finland and Alaska and claim declining case numbers in more recent years in specific locations despite the global increase (Von Bonsdorf 1964). Without targeted studies, the infections could be overlooked as the symptoms are nonspecific. *Dibothriocephalus* spp. can be inactivated with prolonged freezing periods (i.e., below −20 °C for 7 days or below −35 °C for 15 h) and with cooking (56 °C for 5 min) (FDA 1998; Wharton and Aalders 2002).

2.5 Geographic Information

Dibothriocephalus spp. (formerly *Diphyllobothrium* spp.) are found worldwide with documented human infections in Europe, Asia, and North and South America (Oshima 1972; Sagua et al. 2001; Dupouy-Camet and Peduzzi 2004). In many cases, the parasite is considered endemic within the aquatic life, but there has been at least one instance thought to have been an anthropogenic introduction into South America from European immigrants (Semenas and Úbeda 1997). In Finland, although the parasite is present throughout the country and environmental conditions are similar, the prevalence of human infections is much higher in eastern Finland where consumption of raw fish is an ancestral practice compared with more western regions of the country where the customs differ (von Bonsdorff 1977).

2.6 Relevance to Arctic Ecosystems

There are concerns about the potential exposure of humans to zoonotic parasites associated with changes in global climate patterns, ocean nutrient levels, and species distributions of intermediate and definitive hosts. Human infections have been associated with imported fish species with molecular analysis necessary for teasing out sources of infection (Greigert et al. 2020). Changes in fish species distributions are currently being observed in the Arctic, especially for salmonids that could have implications for the emergence of human infections (Bilous and Dunmall 2020). Associations between zoonotic marine parasite levels and climatic features, such as the *El Niño*-Southern Oscillation, have been found in coastal regions of South

America (Arriaza et al. 2010). As the climate warms in the Arctic, changes in species distributions are being observed, including the introduction of new potential intermediate hosts and new species of parasites into that region (Chueng et al. 2009). It is likely that human and animal cases of diphyllobothriasis are underdiagnosed, and this zoonosis is expected to continue to be considered a (re)-emerging disease of concern associated with human preferences of consuming raw or undercooked fish, global trade of fish products, and globalized human movement (Scholz and Kuchta 2016).

3 Conclusions

The human incidence of anisakiasis and diphyllobothriasis in relation to the consumption of traditionally uncooked fish (i.e., *civeche* in Spanish) has been more extensively studied in South American human populations (Arriaza et al. 2010), as well as targeted studies from Europe (Dupouy-Camet and Peduzzi 2004), Asia (i.e., sushi in Japan; Nawa et al. 2001), and parts of North America (from travel and consumption of wild and reared fish (Deardorff and Overstreet 1991; Dick et al. 2001; Dick 2008). The significance of these parasites to humans and wildlife in the Arctic is currently poorly understood. In general, research gaps exist to understand their molecular identity, host range, geographic range, prevalence, incidence, and significance in Arctic environments. Effective treatments (e.g., anthelminthics such as praziquantel) are available for diagnosed infections in people and domestic animals. Avoiding consumption of raw or undercooked meat (e.g., dried, smoked, or pickled) would prevent human disease, and avoiding feeding raw fish to domestic animals, such as dogs and cats, would also decrease risks for people. However, many of these foods have important sociocultural benefits, and the development of public health messaging regarding the risks of consumption requires collaboration with traditional knowledge holders, communities, and local health authorities. Hunters and fishers may detect the parasites at harvest, with the potential for scientists and governments to work with communities on zoonotic disease education and scientific investigation. Regular deworming is often recommended to dog handlers in communities that feed raw fish to dogs, but many communities do not have regular access to veterinary care. Although the relevance of these guidelines to all cold-adapted species of these parasites is unknown, further investigation and collaborative community-based food safety projects are needed to better meet the needs of northern communities. Knowledge about these parasites will be relevant to any communities wishing to participate in the commercial harvest of marine species with consideration for risk mitigation measures related to sale of the products and protection of the workers from allergic reactions. Control of fecal material from animals and humans in waterways would also be important to limit the number of eggs of these parasites being shed in the environment, as well as multiple other water-borne zoonoses. Human and animal health providers should be aware of these zoonoses and their preventive measures and treatments, as increased detection will improve our understanding of the importance of these parasites in communities and ecosystems.

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